

REMARKS

Upon entry of the foregoing amendment, Claims 1-23 will remain pending in the application. Claim 23 has been withdrawn from consideration. Claims 1, 2, 5, 6, 10, 18, 20 and 21 have been amended. Support for the amended Claim 1 can be found, for example, on page 3, lines 9, lines 25-26 and page 6, lines 9-12. Support for amendments of Claim 2 can be found, for example, on page 4, first full paragraph. Support for amendments of Claim 10 can be found, for example, on page 5, lines 12-18 and examples. These changes do not introduce new matter, and their entry is respectfully requested.

In the Office Action dated April 27, 2009, the Examiner set forth a number of grounds for rejection. These grounds are addressed individually and in detail below.

Species Election

Applicants affirm the species election of “limonene” in Claim 8 and “carvone” in Claim 17 for the initiation of examination.

Further, Claims 22 and 23 do not appear to be currently withdrawn from consideration, Claim 22 has been examined and rejected under 35 U.S.C. § 112, second paragraph. Applicants are requesting the withdrawal of the species requirement on the basis that the Examiner has now initiated examination of additional species (*i.e.* Claim 22).

Claims Rejections Under 35 U.S.C. § 112, First Paragraph (Written Description)

Claims 13 and 14 stand rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth on page 2 of the Office Action. The Examiner states that the present claims contain subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully disagree.

Claim 13 is drawn to the method as recited in Claim 1, wherein the biotransformation is carried out in a medium with a reduced quantity of carbon source. Claim 14 is drawn to the method as recited in Claim 13, wherein the reduced quantity of carbon source is < 50 gL⁻¹.

Applicant respectfully submits that the standard for determining compliance with the Written Description requirement is outlined in the MPEP 2163.02. Whenever the issue arises, the fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. See, e.g., *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). The specification teaches the advantage of the claimed method wherein the biotransformation reaction is carried out in a medium containing a reduced quantity of the otherwise convention carbon source (see page 5, last 5 lines and page 6, lines 21-28 of the specification). A medium for growing microorganisms is well known in the art. The subject matter of the claim need not be described literally (*i.e.*, using the same terms or *in haec verba*) in order for the disclosure to satisfy the description requirement (MPEP 2163). Therefore, any medium, known to be used for microorganisms, containing a reduced carbon source, preferable at the concentration claimed and supported in the specification satisfies the requirement for determining compliance with the Written Description requirement.

It is believed that the grounds for the rejection have been obviated, and withdrawal of the rejections under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Claims Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 1-22 stand rejected under 35 U.S.C. § 112, second paragraph, for being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention, for the reasons set forth on pages 2-4 of the Office Action.

Specifically, the Examiner states that the claims have no active steps and are confusing for reciting the term “terpene hydrocarbon”. Independent Claim 1 has been amended to recite “active steps” and amended to recite **oxidized** flavor-active terpenes to differentiate from the term “terpene hydrocarbons”.

Applicants respectfully submit that the word “mycel” is well known in the scientific community, however to advance the prosecution, Applicants have amended the claims to recite “*mycelium*”.

With regards to Claim 2, the Examiner states that the claim does not have an active step and it cannot be determined where in the process the ultrasonication occurs. Claim 2 has been amended to recite “ultrasonic treatment and/or extrusion can be performed before or after the method step (a).

The Examiner states that the Claim 6 recites *Fusarium proliferatus*, which is not a fungi. Claim 6 has been amended to address the Examiner’s concerns.

The Examiner states that the Claim 10 recites that induction by substrate addition is carried out in the lyophilized mycel, however, in example, the induction is not carried out in the mycel when in the lyophilized state. Claim 10 has been amended to recite “before the biotransformation an enzyme induction is carried out in the mycelium prior to lyophilization”.

The Examiner states that the Claim 13 is indefinite for reciting the variable M. In response to the Examiner's concerns, the Examiner is directed to the last paragraph on page 5 where it is defined that M stands for quantity.

The Examiner states that the Claim 21 has two periods in it and it is unclear what is "Pleurotus spec." Claim 21 has been amended to recite "species of the genus *Pleurotus*".

The Examiner states the claims should be redrafted using italicized genus and species names. Applicants submit that all of the genus and species names in the claims have been italicized.

The Examiner states Claims 1-22 are incomplete for omitting essential steps. The omitted step is a step of recovering of the product. In response to this rejection, Claims 1-22 have been amended to recite a step of recovery of the product.

In view of the foregoing, Applicants respectfully submit that the grounds for this rejection have been obviated and that withdrawal of the rejections 35 U.S.C. § 112, second paragraph is respectfully requested.

Claims Rejections Under 35 U.S.C. § 103(a)

Claims 1-19 and 21 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Onken et al. (hereinafter "Onken") in view of Sundari et al. (hereinafter "Sundari") or the ATCC Catalog and Taubert et al. (hereinafter "Taubert") for the reasons set forth on pages 4-6 of the Office Action. Claim 20 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Onken in view of Sundari or the ATCC Catalog and Taubert as applied to Claims 1-19 and 21 above, and further in view of Kaspera et al. (hereinafter "Kaspera") for reasons set forth on page 6. Applicants respectfully traverse the rejections.

To establish a *prima facie* case of obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F. 2d981, 180 USPQ 580 (CCPA, 1074).

The present independent Claim 1, as amended, is directed to A method for producing oxidized flavor-active terpenes from terpene hydrocarbon substrates by means of a selective biotransformation-using microorganisms of the *ascomycetes*, *basidiomycetes* and *deuteromycetes* classes, comprising: (a) providing a lyophilized mycelium, (b) rehydrating the lyophilized mycelium, (c) mixing the rehydrated mycelium from step (b) with the substrate, and (d) recovering the oxidized flavor-active terpene.

Onken generally describes that the production of the terpene carvone from the terpene hydrocarbon limonene via biotransformation with the basidiomycete, *Pleurotus sapidus*. Onken uses a preculture in his method, in which preparation is not disclosed in Onken (see page 164, right column, item 2.2, "Cultivation", "Precultures"). In contrast, the present claimed method uses a microorganism that is added in the form of a lyophilized *mycelium* which is rehydrated.

The present specification further describes that the biotransformation with subsequent lyophilization and rehydrating of the *mycelium* performed more effectively than with the methods disclosed in the prior art. Particularly, the present claimed method can be performed within 24 hours with 150 rpm at 24°C (see Example 1 of the specification). In contrast, in the method of Onken, the production of flavor-active terpenes is performed over several days (see page 165, Figure 2 of Onken). In addition, Onken uses fungi cultures as starting material that have been precultivated for 2.5 days in advance of the biotransformation (see page 165, 2nd paragraph of Onken).

Therefore, Onken does not teach or suggest a process for the biotransformation by using a lyophilized *mycelium* as recited in the claims. Onken only uses intact cells, and a person of ordinary skill in the art would not be motivated to alter the cell membranes via lyophilization as claimed.

Sundari as well as the ATTC Catalog disclose that *mycelium* of different fungi may be lyophilized for storage reasons. Sundari discloses that the *mycelium* of some of the fungi maintained their viability and growth behavior after the lyophilization process. Neither Sundari nor the ATCC Catalog teaches or suggests that the rehydrated cells are capable of transforming terpene hydrocarbons to oxidized flavor-active terpenes according to the claimed invention. Thus, these documents only provide that lyophilization of *mycelium* from fungi and subsequent rehydration restores the enzyme systems that are necessary for viability and growth of the fungi. However, as indicated in the paragraph of pages 1 and 2 of the present specification, the monoterpenes and sesquiterpenes are used as products of the secondary metabolism in the plant world. Secondary metabolites are usually not necessary for the viability and growth behavior of an organism. Therefore, the skilled person would not be able to conclude from Sundari, that the lyophilization and subsequent hydration would also restore enzyme systems that are necessary for the production of secondary metabolites.

Accordingly, the present application has shown that the lyophilization and subsequent rehydration in *mycelium* of fungi do restore the enzyme systems that are necessary for biotransformation of secondary metabolites in an optimal way without the cell membrane negatively influencing the metabolite transport into and out of the cell. Thus, it is not obvious to one skilled in the art to derive the present claimed invention from Sundari and ATTC Catalog.

Taubert generally describes the release of active enzymes from filamentous fungi without enzyme degradation and any loss of enzyme activity. In contrast, the present claimed invention does not work with enzymes being released into the cell culture medium but with the starting compounds, *i.e.*, the terpene hydrocarbons penetrating the cell wall and diffusing into the cells of the fungi (see page 4, 3rd paragraph of the specification). In fact the teachings of Taubert would lead away from the present claimed invention. In particular, Taubert concludes that lyophilization and ultra-turrax treatment are disadvantageous in releasing enzymes from fungi (see page 229, left column and page 230, right column, 1st paragraph of Taubert).

Thus, Onken, which relates to the production of the terpenes via biotransformation provides no motivation to combine Sundari and ATTC Catalog which describe that *mycelium* of different fungi may be lyophilized for storage reasons, while maintaining viability, since none of the references predictably teaches or suggests the effect of lyophilization and subsequent hydration for the production of secondary metabolites. Furthermore, neither Onken nor Sundari and ATTC Catalog provide motivation to combine Taubert since Taubert discloses the disadvantages of lyophilization and ultra-turrax treatment on releasing enzymes from fungi, as discussed above.

Lastly, Kaspera does not cure the deficiency of Onken, Sundari, ATCC Catalog and Taubert because Kaspera also fails to teach or suggest a process for the claimed biotransformation by using a lyophilized *mycelium* as recited in the claim.

Therefore, Claim 1 is patentable over Onken in view of Sundari or the ATCC Catalog and Taubert because the cited references, individually or in combination, fail to teach or suggest all of the claim limitations.

Claims 2-22 are also patentable because they depend from Claim 1, and recite additional patentable subject matter.

In view of the foregoing, Applicants respectfully submits these grounds of rejection have been obviated and withdrawal of the rejection under 35 U.S.C. §103 is respectfully requested.

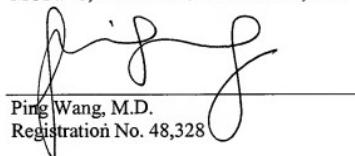
CONCLUSION

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action and, as such, the present application is in condition for allowance.

If the Examiner believes, for any reason, that personal communication will expedite prosecution of the application, the Examiner is invited to contact Applicants' counsel, Ping Wang, M.D. (Reg. No. 48,328), at 202.842.0217.

Respectfully submitted,

MORRIS, MANNING & MARTIN, LLP



Ping Wang, M.D.
Registration No. 48,328

1333 H Street, N.W.
Suite 820
Washington, D.C. 20005
Telephone No. 202.842.0217
Facsimile No. 202.408.5146